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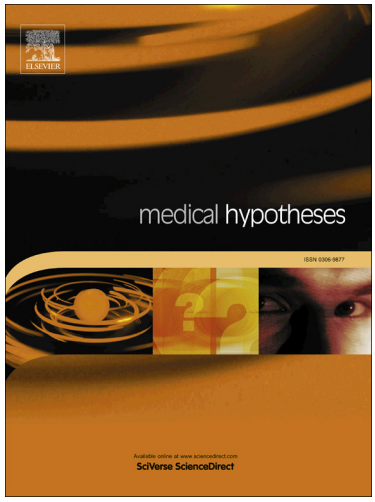

Are non-communicable diseases chronically communicable: a role for the human microbiota?

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Are non-communicable diseases chronically communicable: a role for the human microbiota?

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There is increasing amount of information about the role of gut microbiome composition in communicable –or infectious diseases– and antibiotic resistance, but also how the human microbiota can be involved in chronic non-communicable diseases (NCDs) like diabetes and diabetes-related endophenotypes.(1) While much interest has recently been awakened that perturbations in gut microbiota are associated with the burden of antibiotic resistance(2), recent efforts investigating the potential causal effects or predictive value of information on the composition of microbiota, or their metabolites (e.g., Trimethylamine N-oxide (TMAO) in the circulation) or their functions (like changes in the gut-blood barrier (GBB) permeability) will open new avenues of research.(3-5)

Recently, experimental studies demonstrated how administration of *Akkermansia muciniphila*, one of the most abundant members of the human gut microbiota, to mice can prevent the development of obesity and associated complications.(3) In other words, pasteurization of *A. muciniphila* enhances its capacity to reduce insulin resistance and dyslipidemia in mice.(3) These findings were in line with previous evidence that microbiota transfer from adult male to female mice yielded in protection against diabetes development.(6) Moreover, there is evidence in human adults how taking metformin can influence the several microbial populations such as an increase in *A.muciniphila*.(7) As such evidence in human studies provides valuable insights into our understanding of metabolic disorders, it is time to re-think about the underlying host gene-environment and host-microbiome interactions to explore missing players and predictors for the prevention and treatment of non-communicable diseases.

So far, epidemiological observations or clinical trials have been mainly focused on genes, endophenotypes and the host gene- environment interactions.(8) Research studies in humans show that the host-microbiome communication is essential to maintain vital functions

of the healthy human over the life course.(1, 8) Therefore, the effect estimates (for human genes, biomarkers or interventions) obtained in the classical settings can be modified if one could take into account the transmission of human microbiota between people within a certain population.(1, 9, 10) Given the fact that microbiome traits are considered heritable and the trait associations tend to be small(8), complementary evidence from an integrative analysis of how the host gene-environment interaction can influence diversity and structure of the human microbiome and vice versa may find right matched pieces of the puzzle in these diseases.

Another aspect of research for microbiome-disease associations is to investigate whether additional information on the composition and structure of the human microbiota is of value to improve the risk prediction for NCDs. In this context, the performance of prediction models including classical risk factors and the utility of microbiome traits needs to be formally quantified using prognostic metrics and clinical reclassification. (11, 12). Few out of several studies on microbiota metabolites or functions have conducted a formal quantification to support predictive utility of these phenotypes for NCDs.(4, 5)

So, future lines of research need to focus on two hypotheses; human microbiota or a panel of microbiota-related phenotypes would improve risk prediction or be causally associated with NCDs. Such complementary strands of evidence may demonstrate if information about human microbiota can serve as prognostic markers for predicting clinical health outcomes and behavior; or as novel targets for new therapeutic and prevention strategies in clinical or public health practice.

Conflict of Interest Disclosures:

The author has no competing interests.

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References:

[1] B.O. Schroeder and F. Backhed, Signals from the gut microbiota to distant organs in physiology and disease, *Nature medicine* **22** (2016), pp. 1079-1089.

[2] E. van Nood, A. Vrieze, M. Nieuwdorp, *et al.*, Duodenal infusion of donor feces for recurrent Clostridium difficile, *The New England journal of medicine* **368** (2013), pp. 407-415.

[3] H. Plovier, A. Everard, C. Druart, *et al.*, A purified membrane protein from Akkermansia muciniphila or the pasteurized bacterium improves metabolism in obese and diabetic mice, *Nature medicine* (2016).

[4] M. Ufnal and K. Pham, The gut-blood barrier permeability - A new marker in cardiovascular and metabolic diseases?, *Medical hypotheses* **98** (2017), pp. 35-37.

[5] X.S. Li, S. Obeid, R. Klingenberg, *et al.*, Gut microbiota-dependent trimethylamine N-oxide in acute coronary syndromes: a prognostic marker for incident cardiovascular events beyond traditional risk factors, *European heart journal* (2017).

[6] J.G. Markle, D.N. Frank, S. Mortin-Toth, *et al.*, Sex differences in the gut microbiome drive hormone-dependent regulation of autoimmunity, *Science (New York, N.Y.)* **339** (2013), pp. 1084-1088.

[7] J. de la Cuesta-Zuluaga, N.T. Mueller, V. Corrales-Agudelo, *et al.*, Metformin Is Associated With Higher Relative Abundance of Mucin-Degrading Akkermansia muciniphila and Several Short-Chain Fatty Acid-Producing Microbiota in the Gut, *Diabetes care* **40** (2017), pp. 54-62.

[8] A.K. Benson, The gut microbiome-an emerging complex trait, *Nature genetics* **48** (2016), pp. 1301-1302.

[9] G. Musso, R. Gambino and M. Cassader, Obesity, diabetes, and gut microbiota: the hygiene hypothesis expanded?, *Diabetes care* **33** (2010), pp. 2277-2284.

[10] H.J. Harmsen and M.C. de Goffau, The Human Gut Microbiota, *Advances in experimental medicine and biology* **902** (2016), pp. 95-108.

[11] A. Abbasi, L.M. Peelen, E. Corpeleijn, *et al.*, Prediction models for risk of developing type 2 diabetes: systematic literature search and independent external validation study, *BMJ (Clinical research ed.)* **345** (2012), p. e5900.

[12] K.G. Moons, D.G. Altman, J.B. Reitsma, *et al.*, Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD): explanation and elaboration, *Ann Intern Med* **162** (2015), pp. W1-73.